

(12) DEMANDE INTERNATIONALE PUBLIÉE EN VERTU DU TRAITÉ DE COOPÉRATION  
EN MATIÈRE DE BREVETS (PCT)

26 JAN 2005

(19) Organisation Mondiale de la Propriété  
Intellectuelle  
Bureau international



(43) Date de la publication internationale  
5 février 2004 (05.02.2004)

PCT

(10) Numéro de publication internationale  
WO 2004/011464 A3

(51) Classification internationale des brevets<sup>7</sup> :  
C07D 487/04, C07H 17/02, A61K 31/53, 31/70, A61P  
25/00, 35/00, 31/00 // (C07D 487/04, 251:00, 231:00)

(21) Numéro de la demande internationale :  
PCT/FR2003/002354

(22) Date de dépôt international : 25 juillet 2003 (25.07.2003)

(25) Langue de dépôt : français

(26) Langue de publication : français

(30) Données relatives à la priorité :  
02/09519 26 juillet 2002 (26.07.2002) FR

(71) Déposant (pour tous les États désignés sauf US) :  
GREENPHARMA [FR/FR]; Biopole Clermont Limagne,  
F-63360 Saint Beauzire (FR).

(72) Inventeurs; et

(75) Inventeurs/Déposants (pour US seulement) :  
BERNARD, Philippe [FR/FR]; 16, rue des Lilas,  
F-18800 Farges-en-Septaine (FR). RABOISSON, Pierre  
[FR/FR]; 26, rue de la Chênaie, F-67201 Eckbolsheim  
(FR). JOSEPH, Benoît [FR/FR]; Résidence les Tamaris,  
Appartement 624, 36, rue des Antonins, F-69100 Villeur-  
banne (FR).

(74) Mandataires : MARTIN, Jean-Jacques etc.; Cabinet  
Regimbeau, 20, rue de Chazelles, F-75847 Paris Cedex 17  
(FR).

(81) États désignés (national) : AE, AG, AL, AM, AT, AU, AZ,  
BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ,  
DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,  
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,  
US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) États désignés (régional) : brevet ARIPO (GH, GM, KE,  
LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), brevet  
eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), brevet  
européen (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
TR), brevet OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

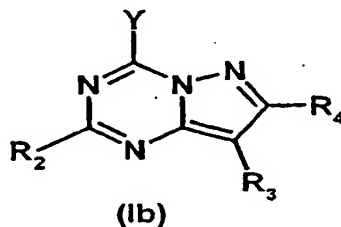
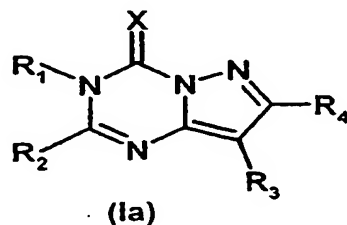
Publiée :

— avec rapport de recherche internationale  
— avant l'expiration du délai prévu pour la modification des  
revendications, sera republiée si des modifications sont re-  
çues

[Suite sur la page suivante]

(54) Title: NOVEL SUBSTITUTED PYRAZOLO[1,5-*a*]-1,3,5-TRIAZINE DERIVATIVES AND THEIR ANALOGUES,  
PHARMACEUTICAL COMPOSITIONS CONTAINING SAME, USE THEREOF AS MEDICINE AND METHODS FOR  
PREPARING SAME

(54) Titre : NOUVELLES PYRAZOLO[1,5-*a*]-1,3,5-TRIAZINES SUBSTITUÉES ET LEURS ANALOGIQUES, COMPOSI-  
TIONS PHARMACEUTIQUES LES CONTENANT, UTILISATION A TITRE DE MEDICAMENT ET PROCÉDES POUR LEUR  
PREPARATION



(57) Abstract: The invention concerns novel substituted pyrazolo[1,5-*a*]-1,3,5-triazine derivatives and some of their structural analogues, and their therapeutic uses, more particularly for preventing and treating pathologies involving central and/or peripheral neuronal degeneration. The invention also concerns methods for preparing same and novel synthesis intermediates. The compounds of the invention correspond more particularly to general formulae (Ia) and (Ib).

(57) Abrégé : L'invention concerne notamment de nouveaux dérivés de pyrazolo[1,5-*a*]-1,3,5-triazines ainsi que certains de leurs analogues structuraux et leurs applications dans le domaine thérapeutique tout particulièrement pour la prévention et le traitement de pathologies impliquant une dégénérescence des neurones centraux et/ou périphériques. Elle concerne également des procédés pour leur préparation et de nouveaux intermédiaires de synthèse. Les composés de l'invention répondent plus particulièrement aux formules générales (Ia) et (Ib).

*En ce qui concerne les codes à deux lettres et autres abréviations, se référer aux "Notes explicatives relatives aux codes et abréviations" figurant au début de chaque numéro ordinaire de la Gazette du PCT.*

PCT/FR 03/02354

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D487/04 C07H17/02 A61K31/53 A61K31/70 A61P25/00  
 A61P35/00 A61P31/00  
 //(C07D487/04,251:00,231:00)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | WO 99/38868 A (DU PONT PHARM CO)<br>5 August 1999 (1999-08-05)<br>cited in the application<br>examples 3A et 6A<br>claims 1,7 | 1,3                   |
| A          |   | 1,12,15               |
| X          | WO 01/23388 A (NEUROGEN; PFIZER)<br>5 April 2001 (2001-04-05)<br>examples 5C ET 6C<br>-----<br>-/-                            | 3                     |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"G" document member of the same patent family

Date of the actual completion of the international search

8 March 2004

Date of mailing of the international search report

16.06.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax (+31-70) 340-3016

Authorized officer

Alfaro Faus, I

Renseignements relatifs aux membres de familles de brevets

Demande internationale No

PCT/FR 03/02354

| Document brevet cité<br>au rapport de recherche |   | Date de<br>publication | Membre(s) de la<br>famille de brevet(s) | Date de<br>publication |
|---|---|------------------------|---|------------------------|
| WO 9938868                                      | A | 05-08-1999             | US 6191131 B1                           | 20-02-2001             |
|   |   |                        | US 6313124 B1                           | 06-11-2001             |
|   |   |                        | US 6060478 A                            | 09-05-2000             |
|   |   |                        | AT 264860 T                             | 15-05-2004             |
|   |   |                        | AU 748818 B2                            | 13-06-2002             |
|   |   |                        | AU 2478799 A                            | 16-08-1999             |
|   |   |                        | BR 9908206 A                            | 05-12-2000             |
|   |   |                        | CA 2314613 A1                           | 05-08-1999             |
|   |   |                        | CN 1137123 C                            | 04-02-2004             |
|   |   |                        | DE 69916578 D1                          | 27-05-2004             |
|   |   |                        | EP 1344779 A1                           | 17-09-2003             |
|   |   |                        | EP 1049699 A1                           | 08-11-2000             |
|   |   |                        | JP 2002501922 T                         | 22-01-2002             |
|   |   |                        | NZ 505079 A                             | 29-08-2003             |
|   |   |                        | NZ 524842 A                             | 31-10-2003             |
|   |   |                        | PL 342183 A1                            | 21-05-2001             |
|   |   |                        | TW 520372 B                             | 11-02-2003             |
|   |   |                        | WO 9938868 A1                           | 05-08-1999             |
|   |   |                        | US 6358950 B1                           | 19-03-2002             |
|   |   |                        | US 2003008885 A1                        | 09-01-2003             |
| WO 0123388                                      | A | 05-04-2001             | AU 7737900 A                            | 30-04-2001             |
|   |   |                        | BG 106507 A                             | 29-12-2002             |
|   |   |                        | CA 2379633 A1                           | 05-04-2001             |
|   |   |                        | CN 1377355 T                            | 30-10-2002             |
|   |   |                        | CZ 20021089 A3                          | 13-11-2002             |
|   |   |                        | EP 1218381 A2                           | 03-07-2002             |
|   |   |                        | HU 0203131 A2                           | 28-01-2003             |
|   |   |                        | JP 2003510326 T                         | 18-03-2003             |
|   |   |                        | NO 20021357 A                           | 23-05-2002             |
|   |   |                        | PL 354982 A1                            | 22-03-2004             |
|   |   |                        | WO 0123388 A2                           | 05-04-2001             |
|   |   |                        | US 6476038 B1                           | 05-11-2002             |
|   |   |                        | ZA 200202517 A                          | 28-03-2003             |
|   |   |                        |   |                        |
| WO 0250079                                      | A | 27-06-2002             | FR 2818278 A1                           | 21-06-2002             |
|   |   |                        | AU 2509602 A                            | 01-07-2002             |
|   |   |                        | CA 2432417 A1                           | 27-06-2002             |
|   |   |                        | EP 1345941 A1                           | 24-09-2003             |
|   |   |                        | WO 0250079 A1                           | 27-06-2002             |
|   |   |                        | US 2004048849 A1                        | 11-03-2004             |
| FR 2230366                                      | A | 20-12-1974             | CH 581137 A5                            | 29-10-1976             |
|   |   |                        | AU 6925974 A                            | 27-11-1975             |
|   |   |                        | DD 113907 A5                            | 05-07-1975             |
|   |   |                        | DE 2424334 A1                           | 19-12-1974             |
|   |   |                        | FI 146174 A                             | 23-11-1974             |
|   |   |                        | FR 2230366 A1                           | 20-12-1974             |
|   |   |                        | JP 50019769 A                           | 01-03-1975             |
|   |   |                        | NL 7406641 A                            | 26-11-1974             |
|   |   |                        | BE 815405 A1                            | 22-11-1974             |
|   |   |                        | ES 426482 A1                            | 01-09-1976             |
|   |   |                        | ZA 7403316 A                            | 28-01-1976             |
|   |   |                        |   |                        |
| WO 02072202                                     | A | 19-09-2002             | CA 2440553 A1                           | 19-09-2002             |
|   |   |                        | EE 200300435 A                          | 15-12-2003             |
|   |   |                        | EP 1368094 A1                           | 10-12-2003             |
|   |   |                        | HR 20030822 A2                          | 30-04-2004             |

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see supplementary sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
3 & 4 (in part) , 12-18 (in part)

Remark on Protest

☐  
☐

- The additional search fees were accompanied by the applicant's protest.  
No protest accompanied the payment of additional search fees.